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| <b>(54) Title:</b> METHODS AND COMPOSITIONS FOR INHIBITING DEPOSIT FORMATION ON CONTACT LENSES   |           |   |
| <b>(57) Abstract</b><br><br>Methods and compositions for inhibiting the formation of proteinaceous and/or lipid deposits on a contact lens are disclosed. In one embodiment, the present method comprises contacting a contact lens being worn in a mammalian eye with at least one ophthalmically acceptable thiol component in an amount effective to inhibit the formation of at least one of proteinaceous deposits and lipid deposits on the contact lens.  |           |   |

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METHODS AND COMPOSITIONS  
FOR INHIBITING DEPOSIT  
FORMATION ON CONTACT  
LENSES

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Background of the Invention

This invention relates to methods and compositions for inhibiting deposit formation on contact lenses. More particularly, the invention relates to methods and compositions for inhibiting the formation of proteinaceous deposits and/or lipid deposits on contact lenses being worn in mammalian, preferably human, eyes. The use of contact lenses for vision correction is widespread and provides substantial advantages. However, one problem that is apparent is the lack of comfort in wearing contact lenses over long periods of time, even though the lenses themselves are removed from the eye on a regular and frequent basis. One reason for this eye discomfort and irritation is the formation of deposit material on the contact lenses during wear. Such deposit material, which often has its origin in proteinaceous and/or lipid material from the eye of the contact lens wearer, becomes deposited on the contact lens and creates irregularities on the surface of the lens which tend to cause eye discomfort and/or irritation.

One approach to removing the deposit material from contact lenses is to clean the lens of such deposit material while the lens is outside of the eye and not in use. This approach, although very useful, does require an additional step to be implemented by the wearer of the contact lens. It would be advantageous to provide a system whereby the formation of deposit material on a contact lens is inhibited during use of the contact lens.

Of course, any components or materials which are to be used while the contact lens is in the eye must be ophthalmically acceptable. By "ophthalmically acceptable" is meant that a material has  
5 substantially no detrimental effect on the mammalian eye into which it is placed.

Japanese patent application JP-196378 discloses an eye lotion useful as a remedy for cataract. The lotion contains oxidative glutathione as a prodrug  
10 for reduction-type glutathione which plays a role in maintaining transparency of the natural crystalline lens. This patent application does not disclose any effect of the eye lotion on the wearing of contact lenses.

15 Japanese patent application JP-011497 discloses ophthalmic compositions for treatment of corneal diseases which contain oxidized form glutathione or its salts as principal components. These compositions are disclosed as having a pH which is  
20 adjusted at 5.0 and as being useful for the treatment of corneal diseases, e.g., keratitis. This application teaches that conventional auxiliaries may be added, for example, polyvinyl alcohol as a thickener. This application does not teach or suggest  
25 any effective use of such compositions in contact lens care.

Garabedian et al U.S. Patent 4,443,432 discloses a stable sterile two part system for preparing an ocular irrigating solution for irrigating the eye  
30 during surgery. Part A involves a basic solution containing bicarbonate ion. Part B includes an acidic solution containing calcium ions, magnesium ions, dextrose and glutathione provided that one of the solutions contains sodium, potassium and chloride

ions. This patent does not teach or suggest such compositions as being effective for any purpose in the contact lens care context.

Schachar U.S. Patent 4,620,979 discloses a method for maintaining normal ascorbate levels in ocular tissue of an eye subjected to intraocular surgery which involves irrigating the eye with a composition comprising sodium chloride, potassium chloride, calcium chloride, magnesium chloride hydrate, sodium hydrogen phosphate, sodium dihydrogen phosphate, sodium bicarbonate, glucose, adenosine, glutathione, sodium acetate, sodium citrate, sodium lactate and ascorbate. This patent does not teach or suggest any effective use of this composition in the contact lens care context.

There continues to be a need for a system useful to inhibit the formation of deposits on contact lenses.

#### Summary of the Invention

New methods and compositions for inhibiting deposit formation on contact lenses have been discovered. These methods and compositions are very effective for inhibiting the formation of proteinaceous deposits and/or lipid deposits on contact lenses being worn in mammalian, preferably human, eyes. Thus, this inhibiting effect occurs while the lens is in use in the mammalian eye. The present methods and compositions preferably also include one or more components which act on the contact lens to enhance the wearability of the lens, thus making it yet more comfortable for the lens wearer. The present compositions are ophthalmically acceptable, and are easily used to provide an effective amount of the composition to achieve the

desired deposit formation inhibiting effect.

In one embodiment, the present methods for inhibiting the formation of proteinaceous deposits and/or lipid deposits on a contact lens comprise  
5 contacting the contact lens being worn in a mammalian eye with at least one ophthalmically acceptable thiol compound in an amount effective to inhibit the formation of proteinaceous deposits and/or lipid deposits on the contact lens.

10 The present compositions comprise an ophthalmically acceptable carrier component; at least one ophthalmically acceptable wearability component in an amount effective to act, for example, on a contact lens being worn in a mammalian eye, so as to  
15 enhance the wearability of the contact lens; and at least one ophthalmically acceptable thiol component in an amount effective to inhibit the formation of at least one of proteinaceous deposits and lipid deposits on a contact lens being worn in a mammalian  
20 eye.

The present methods and compositions provide for very useful and effective inhibition of contact lens deposit formation. Moreover, the present invention can be very conveniently employed by a contact lens  
25 wearer. For example, the present compositions can be conveniently topically applied to, introduced into, the eye wearing a contact lens to provide the desired deposit formation inhibition.

#### Detailed Description of the Invention

30 The present invention is applicable to all types of contact lenses on which proteinaceous deposits and/or lipid deposits tend to form during use in a mammalian eye. Such lenses, e.g., conventional soft contact lenses, RGPs and hard contact lenses, may be

made of any suitable material or combination of materials and may have any suitable configuration.

One of the important features of the present invention is the use of at least one ophthalmically acceptable thiol component in an amount effective to inhibit the formation of at least one of proteinaceous deposits and lipid deposits on a contact lens being worn in a mammalian eye. Without wishing to limit the invention to any particular theory of operation, it is believed that the thiol component acts to effectively interrupt or disrupt the formation of the proteinaceous and/or lipid deposit material prior to it being deposited on the contact lens being worn. Thus, in one embodiment, the present invention involves methods for inhibiting the formation of deposits on a contact lens being worn in a mammalian eye. These methods comprise contacting this contact lens with at least one ophthalmically acceptable thiol component in an amount effective to inhibit the formation of at least one proteinaceous deposits and lipid deposits on the contact lens. Any suitable ophthalmically acceptable thiol component may be utilized in the present invention, provided that it functions as described herein and has no substantial detrimental effect on the contact lens being worn or on the eye or person of the mammal wearing the contact lens. Preferably, the thiol component is soluble in the presently useful compositions. In general, the thiol components include thiols, salts of thiols, precursors of thiols and mixtures thereof. As used herein, the term "precursors" refers to ophthalmically acceptable materials which are converted in the eye to one or more ophthalmically

acceptable thiols (or the identified thiols),  
ophthalmically acceptable thiol salts (or salts of  
the identified thiols) and mixtures thereof.

Examples of useful thiol components include  
5 glutathione (GSH), oxidation-type glutathione (GSSG),  
N-acetylcysteine, thiocetic acid, 2-oxo-thiazolidine-  
4-carboxylic acid, cysteine, glutamylcysteine,  
ethanethiol, 1,4-butanethiol, 2-mercaptoethylether,  
pentaerythretoltetrathiopropionate and acetate,  
10 polyethyleneglycolimercaptoacetate and  
methylthioglycolate, allyl mercaptan, 2-  
mercaptoethanol, 3-mercaptopropanol, 4-  
mercaptobutanol, 1-thioglycerol, thioerythritol, 2,3-  
dimercaptopropanol, pentaerythretolmono (di;  
15 tri)thiopropionate or acetate, thioglycolic acid,  
thioacetic acid, 3-mercaptopropionic acid, thiolactic  
acid, thiomalic acid, thiosuccinic acid,  
thiosalicylic acid, thiobenzoic acid and their  
respective water soluble salts, furfuryl mercaptan,  
20 2-mercaptobenzimidazole, 2-mercaptobenzoxazole, 2-  
mercapto-3-pyridinol, dimethylaminopropanethiol, 2-  
mercaptoethylamine, 2-n-butylaminoethanethiol, and  
the like and mixtures thereof.

In one useful embodiment, the thiol component is  
25 selected from N-acetylcysteine, thiocetic acid, 2-oxo-  
thiazolidine-4-carboxylic acid, cysteine,  
glutamylcysteine and mixtures thereof.

Preferably, the at least one ophthalmically  
acceptable thiol component is selected from the group  
30 consisting of GSH, ophthalmically acceptable salts of  
GSH, GSSG, ophthalmically acceptable salts of GSSG,  
precursors thereof and mixtures thereof, more  
preferably selected from the group consisting of GSH,  
GSSG, ophthalmically acceptable salts thereof and

mixtures thereof and still more preferably from GSH, GSSG and mixtures thereof, especially GSH.

Examples of ophthalmically acceptable anions included in the presently useful ophthalmically acceptable salts useful as thiol components include chloride, bromide, iodide, sulfate, bisulfate, phosphate, acid phosphate, nitrate, acetate, maleate, fumarate, oxalate, lactate, tartrate, citrate, gluconate, saccharate, p-toluene sulfonate and the like.

The presently useful ophthalmically acceptable thiol components are preferably present in an amount in the range of about 0.0001% to about 10%, more preferably about 0.001% to about 0.5%, by weight per volume of ophthalmically acceptable medium or carrier. The ophthalmically acceptable thiol component may be conveniently used in the form of a composition including an ophthalmically acceptable medium or carrier, such as in the form of an artificial tear, an eye drop, a lotion which is topically applied to the eye and the like.

In one particularly useful embodiment, the present method further comprises introducing or instilling a composition, such as described herein, including at least one ophthalmically acceptable thiol component into the mammalian eye wearing the contact lens. For example, an eye drop or drops containing an effective amount of at least one ophthalmically acceptable thiol component may be added to the contact lens-wearing eye one or more times a day, in particular at the time the contact lens is present in the eye, so as to inhibit the formation of proteinaceous deposits and/or lipid deposits on the contact lens being worn.

The compositions of the present invention include an ophthalmically acceptable medium or carrier, preferably an ophthalmically acceptable liquid aqueous medium. This medium may act as a solvent for the other components in the composition. One particularly useful ophthalmically acceptable carrier is water, such as purified water, sterilized water or preserved water.

One or more additional components can be included in the present compositions based on the particular application for which the compositions are formulated. Thus, the present compositions can be formulated as contact lens wetting compositions, contact lens conditioning compositions, contact lens soaking/storage compositions (for use with the lens before and/or after lens wear to condition the lens for comfort and inhibition of deposit formation) artificial tear compositions and the like. Soaking a contact lens, before and/or after lens wear, in the present compositions for a period of time, on the order of at least about 0.5 or about 1 hour, is effective to enhance the wearability of the lens and/or inhibit deposit formation on the lens after the soaked lens is placed in the eye for a period to wear.

In a particularly useful embodiment, the present compositions have a pH of greater than 5.0, preferably up to about 7.0 or about 8.0, more preferably about 5.3 to about 6.0 and still more preferably about 5.5 to about 5.8. The present compositions having such pHs have been found to be very effective in inhibiting proteinaceous and/or lipid deposit formation on the contact lens in the eye while, at the same time, being suitable for use

within the eye without adversely affecting ocular health or causing eye irritation or discomfort. Compositions having lower pH values have a tendency to cause irritation and/or discomfort in a healthy mammalian eye. To stabilize or maintain the composition at the desired pH, an effective amount of at least one buffer component may be included in the composition. The effective amount of buffer component employed to buffer or maintain the formulation at the desired pH can vary widely and depends to a large degree on the particular buffer component employed, as well as the chemical make-up of the composition. However, desirable results have been obtained when the amount of buffering component incorporated into the composition to stabilize the composition at the desired pH is in the range of about 0.005 to about 1 weight/volume percent of the composition.

Any suitable buffer component can be employed which is compatible with the other ingredients of the composition, and which does not have deleterious or toxic properties which could harm the eye or the contact lens being worn. Examples of suitable ophthalmically acceptable buffer components include acetate buffers, citrate buffers, phosphate buffers, borate buffers and mixtures thereof. Specific buffer components useful in the present invention include boric acid, sodium borate, sodium phosphates, including mono, di- and tri-basic phosphates, such as sodium phosphate monobasic monohydrate and sodium phosphate dibasic heptahydrate, and mixtures thereof. It should be noted that any other suitable ophthalmically acceptable buffer components can be employed to maintain the pH of the ophthalmic

composition so that the composition is provided with an acceptable pH, and the before-mentioned buffer components are merely examples of such buffer components.

5           When it is determined that the composition does not have the desired pH value, the pH of the composition can be adjusted by the addition of an effective amount of either a base or an acid, as the case may be. Any suitable base or acid can be  
10 employed to adjust the pH of the composition which does not provide the composition with toxic or deleterious properties which could harm either the contact lens or the eye. An example of a base which can be used to adjust the pH of the composition is 1  
15 N sodium hydroxide; and an example of an acid which can be used to adjust the pH of the composition is 1 N hydrochloric acid.

          The present compositions preferably include at least one ophthalmically acceptable, polymeric  
20 wearability component in an amount effective to act, for example, on a contact lens being worn in a mammalian eye, so as to enhance the wearability of the contact lens in the mammalian eye. Such wearability components may wet (or rewet) the lens,  
25 condition the lens, coat the lens or otherwise interact with the lens to provide the wearer of the lens with an increased degree of lens wearing comfort when present in an eye wearing a contact lens relative to wearing the contact lens in the absence  
30 of the wearability component. The wearability component is a polymeric component, that is, a component which has one or more sub-molecular units which are repeated at least once, preferably at least about 10 times, in each molecule of the polymeric

component.

Among the useful polymeric wearability components which may be included in the present compositions are contact lens wetting (or rewetting) agents, contact lens conditioning agents and the like. Many such agents are conventional and well known in the art of contact lens care.

Useful polymeric contact lens wetting (or rewetting) agents and conditioning agents include, but are not limited to, polyvinyl alcohol, polyoxamers, polyvinyl pyrrolidine, hydroxypropyl methyl cellulose, hydroxyethyl cellulose, other ophthalmically acceptable cellulose derivatives and mixtures thereof.

The wearability component or components are included in the present compositions in an amount effective to impart or provide the desired increase in lens wearability. Such amount or amounts may vary widely depending, for example, on the specific composition being employed, the specific wearability component or components being utilized, the specific wearability result desired and the composition of the contact lens with which the composition is to be utilized. Preferably, the polymeric wearability component is present in an amount in the range of about 0.1% to about 4%, more preferably about 0.3% to about 3%, (weight/volume) of the composition.

Further, one or more additional components may be included in the present compositions to impart or provide at least one beneficial or desired property to the compositions. Such additional components may be selected from components which are conventionally used in one or more contact lens care compositions, in particular in-the-eye contact lens care

compositions. Examples of such additional components include tonicity agents, nutrient agents, antioxidants, and the like. These additional components are each included in the present compositions in an amount effective to impart or provide the beneficial or desired property to the compositions. For example, such additional components may be included in the present compositions in amounts similar to the amounts of such components used in other, e.g., conventional, in-the-eye contact lens care products.

Useful tonicity adjustors include, but are not limited to, sodium chloride, potassium chloride, mannitol, dextrose, glycerin, propylene glycol and mixtures thereof. Such tonicity adjusting components are preferably included in an amount effective to provide the desired tonicity to the composition, preferably an osmolality of at least about 200 mOsmol/kg and more preferably about 250 to about 350 or 400 mOsmol/kg. Preferably the present compositions are substantially isotonic.

Useful viscosity builders include, but are not limited to, hydroxyethyl cellulose, hydroxypropyl methyl cellulose, polyvinyl pyrrolidone, polyvinyl alcohols and mixtures thereof.

Useful antioxidants include, but are not limited to, sodium metabisulfite, sodium thiosulfate, butylated hydroxyanisole, butylated hydroxytoluene and mixtures thereof.

The present compositions can be prepared in any conventional manner, such as by blending or combining the appropriate ingredients together.

The present compositions are preferably substantially free of effective amounts of one or

more ionic surfactants, that is, cationic surfactants, anionic surfactants and/or amphoteric surfactants. Such ionic surfactants may adversely impact the parameters of the contact lens and/or the eye in which the contact lens is worn. Also, the present compositions are preferably substantially free of effective amounts of one or more enzymes, particularly when such compositions are to be applied directly to or in the eye.

The present compositions are particularly effective when applied directly to or in an eye, in particular an eye wearing a contact lens. Thus, the present compositions can be introduced into the eye periodically on a routine basis or on a predetermined schedule. Alternately, the compositions may be used, as needed, to inhibit proteinaceous and/or lipid deposit formation on a contact lens being worn in a mammalian eye.

The following non-limiting examples illustrate certain aspects of the present invention.

#### EXAMPLES 1 TO 8

A series of tests were conducted to determine the effect of glutathione (GSH) on the formation of lysozyme deposits on a contact lens.

Each of these tests was conducted using a conventional soft hydrogel contact lens (having a water constant of about 55% by weight). The lens was placed in a glass vial with 5 ml of an aqueous solution containing 1.00 g/l of lysozyme, with and without other components as shown in the table below. Following a standard in-vitro procedure for the lysozyme coating of contact lenses, the lens/solution combination was heated to 80°C and maintained at this temperature for 60 minutes. Afterwards, the

14

lens/solution combination was cooled to room temperature. The lens was removed from the solution and inspected using a fiber optic illuminator and an ultraviolet light spectrometer set at 280 nm to determine the extent of lysozyme deposition.

Results of these tests were as follows:

| Example        | GSH,<br>mg/l | Glycerol,<br>mg/l | Lysozyme<br>Fiber Optic<br>Illuminator <sup>1</sup>    | Deposition<br>UV<br>Absorbance <sup>2</sup> |
|----------------|--------------|-------------------|--|---|
| 1              | 25           | 25                | None   | 0.077                                       |
| 2              | 25           | 0                 | None   | 0.102                                       |
| 3(Comparative) | 0            | 25                | Heavy  | 0.817                                       |
| 4              | 25           | 100               | Very Light   | 0.095                                       |
| 5(Comparative) | 0            | 100               | Heavy  | 0.787                                       |
| 6(Comparative) | 0            | 0                 | Heavy  | 0.783                                       |
| 7              | 5            | 0                 | Very Light   | 0.427                                       |
| 8              | 50           | 0                 | Very Light<br>Pitch<br>Near Center<br>(Otherwise None) | 0.130                                       |

(1) These results are visual observations using a fiber optic illuminator.

(2) The degree of UV absorbance increases as the amount of lysozyme deposited increases.

These results demonstrate that glutathione (GSH) is effective in inhibiting the deposition of lysozyme, which is denatured by the above-noted heating step, on contact lenses. The denatured lysozyme is a proteinaceous material which is readily deposited on contact lenses in the absence of GSH

(Examples 3, 5 and 6). With glutathione (GSH) present, Examples 1, 2, 4, 7 and 8, the amount of denatured lysozyme deposited is substantially reduced. The presence of glycerol has little or no effect on the degree of denatured lysozyme deposition on the contact lens.

Example 9

An artificial tear formulation is prepared and has the following composition:

|    |                      |                  |
|----|----------------------|------------------|
| 10 | Glutathione(GSH)     | 0.5% by weight   |
|    | Polyvinyl alcohol    |                  |
|    | (20-90 grade)        | 1.4% by weight   |
|    | Polyvinylpyrrolidone | 0.6% by weight   |
|    | Sodium Chloride      | 0.8% by weight   |
| 15 | Hydrochloric acid    | as needed to a   |
|    | Sodium Hydroxide     | pH of 5.5 to 5.8 |
|    | Purified Water       | as needed to     |
|    |                      | make volume      |

This formulation is applied in the form of drops to the eyes of a human wearer of soft hydrogel contact lenses. The drops are applied twice a day, always when the contact lenses are being worn. The lenses are also subjected to frequent, conventional enzymatic cleaning when they are not being worn. Over a period of time, the lens wearer experiences substantially no discomfort and substantially no irritation as the result of contact lens wear.

While this invention has been described with respect to various specific examples and embodiments, it is to be understood that the invention is not limited thereto and that it can be variously practiced within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A method for inhibiting the formation of deposits on a contact lens comprising:  
contacting a contact lens being worn in a mammalian eye with at least one ophthalmically acceptable thiol component in an amount effective to inhibit the formation of at least one of proteinaceous deposits and lipid deposits on said contact lens.
2. The method of claim 1 wherein said at least one ophthalmically acceptable thiol component is selected from the group consisting of glutathione, oxidation-type glutathione, ophthalmically acceptable salts thereof, precursors thereof and mixtures thereof.
3. The method of claim 1 wherein said at least one ophthalmically acceptable thiol component is selected from the group consisting of N-acetylcysteine, thiocetic acid, 2-oxo-thiazolidine-4-carboxylic acid, cysteine, glutamylcysteine and mixtures thereof.
4. The method of claim 1 wherein said at least one ophthalmically acceptable thiol component is selected from the group consisting of glutathione, oxidation-type glutathione, ophthalmically acceptable salts of thereof and mixtures thereof.
5. The method of claim 1 wherein said at least one ophthalmically acceptable thiol component is selected from the group consisting of glutathione, oxidation-type glutathione and mixtures thereof.

6. The method of claim 1 wherein said at least one ophthalmically acceptable thiol component is glutathione.

7. The method of claim 1 which further comprises introducing a composition including said at least one ophthalmically acceptable thiol component into said mammalian eye wearing said contact lens.

8. The method of claim 7 wherein said composition further includes an ophthalmically acceptable aqueous carrier component and has an ophthalmically acceptable pH of greater than 5.0.

9. The method of claim 7 wherein said composition further includes at least one additional component in an amount effective to act to enhance the wearability of said contact lens.

10. The method of claim 9 wherein said at least one additional component is a polymeric component.

11. The method of claim 8 wherein said composition further includes at least one tonicity adjusting component in an amount effective to provide the desired tonicity to said composition.

12. The method of claim 11 wherein said composition further includes at least one additional component in an amount effective to act on said contact lens so as to enhance the wearability of said contact lens.

13. The method of claim 1 wherein said at least one ophthalmically acceptable thiol component is present in an amount effective to inhibit the formation of proteinaceous deposits on said contact  
5 lens.

14. A method for inhibiting proteinaceous deposits on a contact lens comprising:  
introducing into a mammalian eye wearing a contact lens a composition having an ophthalmically  
5 acceptable pH of greater than 5.0 and comprising an ophthalmically acceptable aqueous carrier component, at least one ophthalmically acceptable wearability component in an amount effective to act to enhance the wearability of said contact lens, at least one  
10 ophthalmically acceptable tonicity adjusting component in an amount effective to provide the desired tonicity to said composition, and at least one ophthalmically acceptable thiol component in an amount effective to inhibit the formation of  
15 proteinaceous deposits on said contact lens.

15. A method for conditioning a contact lens comprising:  
soaking a contact lens in a composition comprising an ophthalmically acceptable aqueous  
5 carrier component, at least one ophthalmically acceptable polymeric wearability component in an amount effective to enhance the wearability of said soaked contact lens in a mammalian eye, and at least  
10 one ophthalmically acceptable thiol component in an amount effective to inhibit the formation of at least one of proteinaceous deposits and lipid deposits on said soaked contact lens in a mammalian eye.

16. A composition useful for inhibiting the formation of deposits on a contact lens comprising:  
an ophthalmically acceptable aqueous carrier component;

- 5           at least one ophthalmically acceptable polymeric wearability component in an amount effective to enhance the wearability of the contact lens in a mammalian eye; and  
10           at least one ophthalmically acceptable thiol component in an amount effective to inhibit the formation of at least one of proteinaceous deposits and lipid deposits on the contact lens being worn in a mammalian eye, said composition having an ophthalmically acceptable pH greater than 5.0.

17. The composition of claim 15 wherein said at least one ophthalmically acceptable thiol component is selected from the group consisting of glutathione, oxidation-type glutathione, ophthalmically acceptable  
5       salts thereof, precursors thereof and mixtures thereof.

18. The composition of claim 16 wherein said at least one ophthalmically acceptable thiol component is selected from the group consisting of N-acetylcysteine, thiocetic acid, 2-oxo-thiazolidine-4-  
5       carboxylic acid, cysteine, glutamylcysteine and mixtures thereof.

19. The composition of claim 16 wherein said at least one ophthalmically acceptable thiol component is selected from the group consisting of glutathione, oxidation-type glutathione, ophthalmically acceptable

5 salts of thereof and mixtures thereof.

20. The composition of claim 16 wherein said at least one ophthalmically acceptable thiol component is selected from the group consisting of glutathione, oxidation-type glutathione and mixtures thereof.

21. The composition of claim 16 wherein said at least one ophthalmically acceptable thiol component is glutathione.

22. The composition of claim 16 which further comprises at least one tonicity adjusting component in an amount effective to provide the desired tonicity to said composition.

23. The composition of claim 16 which further comprises at least one buffer component in an amount effective to maintain said composition at the desired pH.

24. The composition of claim 16 wherein said composition has a pH of less than about 8.0.

25. The composition of claim 16 wherein said composition has a pH in the range of about 5.3 to about 6.0.

26. The composition of claim 16 wherein said composition has a pH in the range of about 5.5 to about 5.8.

27. The composition of claim 26 which includes polyvinyl alcohol and polyvinyl pyrrolidone each in

an amount effective to act to enhance the wearability of the contact lens in a mammalian eye.

28. The composition of claim 27 which further comprise sodium chloride in an amount effective to provide the desired tonicity to said composition.

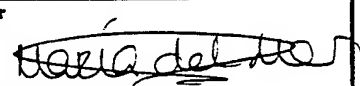
29. A composition useful for inhibiting the formation of deposits on a contact lens comprising:  
an ophthalmically acceptable aqueous carrier component;

5               polyvinyl alcohol and polyvinyl pyrrolidone  
each in an amount effective to act to enhance the wearability of the contact lens in a mammalian eye;  
sodium chloride in an amount effective to provide the desired tonicity to said composition; and  
10               glutathione in an amount effective to inhibit the formation of at least one of proteinaceous deposits and lipid deposits on the contact lens being worn in a mammalian eye, said composition having a pH in the range of about 5.3 to  
15               about 6.0.

## INTERNATIONAL SEARCH REPORT

International Application \*

PCT/US 92/03921

|  |  |                                     |
|--|--|-------------------------------------|
| <b>I. CLASSIFICATION OF SUBJECT MATTER</b> (if several classification symbols apply, indicate all) <sup>6</sup>  |  |                                     |
| According to International Patent Classification (IPC) or to both National Classification and IPC<br>Int.Cl. 5 G02C13/00   |  |                                     |
| <b>II. FIELDS SEARCHED</b>   |  |                                     |
| Minimum Documentation Searched <sup>7</sup>  |  |                                     |
| Classification System  | Classification Symbols   |                                     |
| Int.Cl. 5  | A61L   |                                     |
| Documentation Searched other than Minimum Documentation<br>to the Extent that such Documents are Included in the Fields Searched <sup>8</sup>  |  |                                     |
| <b>III. DOCUMENTS CONSIDERED TO BE RELEVANT<sup>9</sup></b>  |  |                                     |
| Category <sup>10</sup>   | Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>                         | Relevant to Claim No. <sup>13</sup> |
| X  | GB,A,2 019 600 (SENJU SEIYAKU KABUSHIKI KAISHA)<br>31 October 1979<br>see page 1, line 56 - line 60; table 1<br>---                    | 1-6                                 |
| X  | US,A,4 715 899 (SUBIR CHANDA ET AL.) 29 December<br>1987<br>see column 3, line 1 - line 9; claims<br>---                               | 1-6                                 |
| X  | WO,A,8 503 247 (EYE PRODUCTS LIMITED PARTNERSHIP)<br>) 1 August 1985<br>see page 7, line 20 - line 21; claims<br>---                   | 1,3,5                               |
| X  | EP,A,0 219 220 (ALLERGAN PHARMACEUTICALS INC.)<br>22 April 1987<br>see column 9, line 33 - line 43; claims; example<br>1<br>---<br>-/- | 1,3,5                               |
| <p><sup>10</sup> Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&amp;" document member of the same patent family</p> |  |                                     |
| <b>IV. CERTIFICATION</b>   |  |                                     |
| Date of the Actual Completion of the International Search  | Date of Mailing of this International Search Report  |                                     |
| 11 SEPTEMBER 1992  | 23. 09. 92   |                                     |
| International Searching Authority  | Signature of Authorized Officer  |                                     |
| EUROPEAN PATENT OFFICE   | M. ESPINOSA                                       |                                     |

| III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET) |   | Relevant to Claim No. |
|--|---|-----------------------|
| Category <sup>a</sup>  | Citation of Document, with indication, where appropriate, of the relevant passages  |                       |
| X  | FR,A,2 226 677 (ALLERGAN PHARMACEUTICALS) 15<br>November 1974<br>see claims<br>---  | 1,3,5                 |
| X  | JAPANESE PATENTS REPORTS<br>24 July 1986<br>Derwent Publications Ltd., London, GB;<br>& JP,A,61 051 121 (LION CORP.) 13 March 1986<br>see abstract<br>--- | 1,3,5                 |
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| A  | GB,A,2 117 534 (SMITH & NEPHEW ASSOCIATED<br>COMPANIES) 12 October 1983<br>---  |                       |

**ANNEX TO THE INTERNATIONAL SEARCH REPORT  
ON INTERNATIONAL PATENT APPLICATION NO. US 9203921  
SA 60460**

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 11/09/92

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
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